XXX. Normal Mode Analysis

Derivation of the normal mode equation

Assume a protein consists of N atoms. The position of the ith atom is x_i, y_i, z_i. The equilibrium position of ith atom is a_i, b_i, c_i. If a system is in equilibrium, the forces acting on it are equal to zero. The potential energy function can be expanded as a Taylor series around the equilibrium position:

$$\begin{aligned} V(x_1, y_1, z_1; \cdots) = \; & V(a_1, b_1, c_1; \cdots) \\ & + \frac{1}{1!}\left[\left(\frac{\partial V}{\partial x_1}\right)_0 (x_1 - a_1) + \left(\frac{\partial V}{\partial y_1}\right)_0 (y_1 - b_1) + \left(\frac{\partial V}{\partial z_1}\right)_0 (z_1 - c_1) + \cdots\right] \\ & + \frac{1}{2!}\left[\left(\frac{\partial^2 V}{\partial x_1^2}\right)_0 (x_1 - a_1)^2 + 2\left(\frac{\partial^2 V}{\partial x_1\, \partial y_1}\right)_0 (x_1 - a_1)(y_1 - b_1) + \cdots\right] \\ & + \cdots \end{aligned} \tag{1}$$

Since the forces are equal to zero, the first derivatives are zero in eq. 1. From eq. 1, the partial derivatives can be derived as:

$$\begin{aligned} \frac{\partial V}{\partial x_1} \; & \approx \frac{V(x_1, y_1, z_1; \cdots) - V(a_1, b_1, c_1; \cdots)}{x_1 - a_1} \\ & \approx \frac{1}{2}\left(\frac{\partial^2 V}{\partial x_1^2}\right)_0 (x_1 - a_1) + \left(\frac{\partial^2 V}{\partial x_1\, \partial y_1}\right)_0 (y_1 - b_1) + \left(\frac{\partial^2 V}{\partial x_1\, \partial z_1}\right)_0 (z_1 - c_1) \end{aligned}$$

According to Newton's law,

$$m_1 \frac{d^2 x_1}{dt^2} = -\frac{\partial V}{\partial x_1}$$

In matrix form,

$$\begin{bmatrix} m_1 & 0 & 0 & \cdots \\ 0 & m_1 & 0 & \cdots \\ 0 & 0 & m_1 & \cdots \\ & & & \vdots \end{bmatrix} \frac{d^2}{dt^2} \begin{bmatrix} \Delta x_1 \\ \Delta y_1 \\ \Delta z_1 \\ \vdots \end{bmatrix} + \begin{bmatrix} \frac{1}{2}\left(\frac{\partial^2 V}{\partial x_1^2}\right)_0 & \left(\frac{\partial^2 V}{\partial x_1\, \partial y_1}\right)_0 & \left(\frac{\partial^2 V}{\partial x_1\, \partial z_1}\right)_0 & 0 & \cdots \\ \left(\frac{\partial^2 V}{\partial y_1\, \partial x_1}\right)_0 & \frac{1}{2}\left(\frac{\partial^2 V}{\partial y_1^2}\right)_0 & \left(\frac{\partial^2 V}{\partial y_1\, \partial z_1}\right)_0 & 0 & \cdots \\ \left(\frac{\partial^2 V}{\partial z_1\, \partial x_1}\right)_0 & \left(\frac{\partial^2 V}{\partial z_1\, \partial y_1}\right)_0 & \frac{1}{2}\left(\frac{\partial^2 V}{\partial z_1^2}\right)_0 & 0 & \cdots \\ & & & & \vdots \end{bmatrix} \begin{bmatrix} \Delta x_1 \\ \Delta y_1 \\ \Delta z_1 \\ \vdots \end{bmatrix}$$

$$= \mathbf{0}$$

In a compact form,

$$\mathbf{M}\frac{d^2}{dt^2}\mathbf{q} + \mathbf{V}\mathbf{q} = \mathbf{0}$$

or

$$\frac{d^2}{dt^2}\mathbf{q} + \mathbf{H}\mathbf{q} = \mathbf{0} \tag{2}$$

where $\mathbf{H} = \mathbf{M}^{-1}\mathbf{V}$ is called the Hessian matrix.

If

$$\mathbf{H}\mathbf{a}_n = \lambda_n \mathbf{a}_n,$$

then

$$\cos(\sqrt{\lambda_n}t + \delta_n)\mathbf{a}_n$$

is one solution to eq. 2. This implies that the vibration frequency in the direction $\mathbf{a}_n$ is $\sqrt{\lambda_n}$. The eigenvectors of $\mathbf{H}$ are called the normal mode vectors; the corresponding eigenvalues are called normal modes. The modes are the square of the angular frequencies with which the particles vibrate in the direction of the corresponding eigenvectors.

The general solution to eq. 2 has the form

$$\mathbf{q} = \sum_{n=1}^{N} c_n \cos\left(\sqrt{\lambda_n}t + \delta_n\right)\mathbf{a}_n$$

For a large protein, it is difficult to implement the method for two challenges: the determine the equilibrium position; to compute the eigenvectors and eigenvalues.

References

J. A. Bauer, and V. Bauerová-Hlinková, “Normal Mode Analysis: A Tool for Better Understanding Protein Flexibility and Dynamics with Application to Homology Models”, in Homology Molecular Modeling - Perspectives and Applications. London, United Kingdom: IntechOpen, 2020 [Online]. Available: https://www.intechopen.com/chapters/73720 doi: 10.5772/intechopen.94139